

WHAT IS CLAIMED IS:

1. A method of reducing or inhibiting proliferation or metastasis of small-cell lung cancer (SCLC) cells characterized by elevated Hedgehog (Hh) pathway activity as compared with a normal cell, comprising contacting the cells with at least one Hh pathway antagonist, thereby reducing or inhibiting proliferation of the small-cell lung cancer cells.
2. The method of claim 1, wherein the elevated Hh pathway activity comprises elevated ligand stimulated Hh pathway activity.
3. The method of claim 2, wherein the ligand comprises Sonic hedgehog (SHH).
4. The method of claim 1, wherein the elevated Hh pathway activity comprises elevated transcription factor.
5. The method of claim 4, wherein the transcription factor comprises a GLI-1 transcription factor.
6. The method of claim 1, wherein the Hh pathway antagonist comprises a steroidal alkaloid or derivative thereof.
7. The method of claim 6, wherein the steroidal alkaloid is cyclopamine.
8. The method of claim 1, wherein the Hh pathway antagonist is a nucleic acid or a protein molecule.
9. The method of claim 8, wherein the protein molecule is an antibody or binding fragment thereof.
10. The method of claim 1, further comprising contacting the cells with a chemotherapeutic agent.
11. The method of claim 7, further comprising contacting the cells with an antibody or binding fragment thereof.

12. The method of claim 11, wherein the antibody is an anti-Hh antibody.
13. A method of ameliorating small-cell lung cancer in a subject, comprising administering to the subject a Hh pathway antagonist, whereby the Hh pathway antagonist contacts small-cell lung cancer cells in the subject, thereby ameliorating the small-cell lung cancer in the subject.
14. The method of claim 13, wherein the elevated Hh pathway activity comprises elevated ligand stimulated Hh pathway activity.
15. The method of claim 14, wherein the ligand comprises Sonic hedgehog (SHH).
16. The method of claim 13, wherein the elevated Hh pathway activity comprises elevated transcription factor.
17. The method of claim 16, wherein the transcription factor comprises a GLI-1 transcription factor.
18. The method of claim 13, wherein the Hh pathway antagonist comprises a steroidal alkaloid or derivative thereof.
19. The method of claim 18, wherein the steroidal alkaloid is cyclopamine.
20. The method of claim 13, further comprising administering to the subject a chemotherapeutic agent.
21. The method of claim 19, further comprising contacting the cells with an antibody or binding fragment thereof.
22. The method of claim 21, wherein the antibody is anti-Hh antibody.
23. The method of claim 13, wherein the Hh pathway antagonist is administered orally.
24. A method of identifying small-cell lung cancer amenable to treatment with a Hedgehog (Hh) pathway antagonist, comprising detecting elevated Hh pathway activity

in a sample of cells as compared to Hh pathway activity in corresponding normal cells, thereby identifying small-cell lung cancer amenable to treatment with a Hh pathway antagonist.

25. The method of claim 24, wherein the cells are from a biopsy sample obtained from a subject.

26. The method of claim 24, wherein the cells are from a tissue or bodily fluid obtained from a subject.

27. The method of claim 24, wherein the elevated Hh pathway activity comprises ligand stimulated Hh pathway activity.

28. The method of claim 24, comprising detecting elevated expression of at least one Hh pathway polypeptide.

29. The method of claim 28, wherein the Hh pathway polypeptide comprises a Hh ligand, a Hh ligand receptor, or a transcription factor.

30. The method of claim 29, wherein the Hh ligand comprises Sonic hedgehog (SHH).

31. The method of claim 29, wherein the Hh ligand receptor comprises Patched.

32. The method of claim 29, wherein the transcription factor comprises a GLI-1 transcription factor.

33. The method of claim 28, which comprises detecting elevated levels of a polynucleotide encoding the Hh pathway polypeptide.

34. The method of claim 33, wherein the polynucleotide comprises RNA.

35. The method of claim 28, which comprises performing a reverse transcription-polymerase chain reaction.

36. The method of claim 28, which comprises detecting elevated levels of the Hh pathway polypeptide.

37. The method of claim 36, which comprises performing an immunoassay.

38. The method of claim 36, wherein the Hh pathway polypeptide comprises a transcription factor.

39. The method of claim 38, which comprises detecting increased binding activity of the transcription factor to a cognate transcription factor regulatory element.

40. The method of claim 38, which comprises detecting increased expression of a reporter gene comprising a cognate transcription factor regulatory element.

41. The method of claim 24, which comprises detecting altered expression of a transcriptional target of the Hh pathway.

42. The method of claim 41, which comprises detecting increased expression of a gene that is positively regulated by GLI-1.

43. The method of claim 24, further comprising contacting cells of the sample with at least one Hh pathway antagonist, and detecting a decrease in Hh pathway activity in the cells following said contact, thereby confirming that the small-cell lung cancer is amenable to treatment with a Hh pathway antagonist.

44. The method of claim 43, wherein the antagonist is cyclopamine.

45. The method of claim 44, further comprising contacting the cells with a chemotherapeutic agent.

46. The method of claim 44, further comprising contacting the cells with an anti-Hh antibody or binding fragment thereof.

47. A method of identifying an agent useful for treating small-cell lung cancer wherein the small-cell lung cancer cells have elevated Hedgehog (Hh) pathway activity, comprising contacting a sample of small-cell lung cancer cells with at least one test agent,

wherein a decrease in Hh pathway activity in the presence of the test agent as compared to Hh pathway activity in the absence of the test agent identifies the agent as useful for treating small-cell lung cancer.

48. The method of claim 47, wherein the elevated Hh pathway activity comprises elevated ligand stimulated Hh pathway activity.

49. The method of claim 48, wherein the ligand comprises Sonic hedgehog (SHH).

50. The method of claim 47, wherein the elevated Hh pathway activity comprises elevated transcription factor.

51. The method of claim 50, wherein the transcription factor comprises a GLI-1 transcription factor.

52. The method of claim 47, wherein the agent comprises a Hh pathway antagonist.

53. The method of claim 52, wherein the antagonist comprises steroidal alkaloid or a derivative thereof.

54. The method of claim 49, wherein the steroidal alkaloid is cyclopamine.

55. The method of claim 47, which is performed in a high throughput format.

56. The method of claim 55, comprising contacting samples of cells of a plurality of samples with at least one test agent.

57. The method of claim 56, wherein plurality of samples are obtained from a single subject.

58. The method of claim 56, wherein the plurality of samples are obtained from different subjects.

59. A method for monitoring a therapeutic regimen for treating a subject having small-cell lung cancer comprising determining a change in Hh pathway activity during therapy.

60. The method of claim 59, wherein the therapy comprises the treatment of claim 1.